Particulate Matter Triggers Ventricular Arrhythmias Via Carotid Body/Autonomic Dysfunction in a Murine Model of Cardiomyopathy.

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Previous studies report ambient particulate matter (PM) correlates with arrhythmias and sudden death in humans with preexisting cardiac dysfunction, yet the mechanisms behind these changes remain unknown. The effects of ambient PM (10 uM) were assessed in control CD1 and cardiomyopathy prone CREB mice with a cardiac specific promoter mutation in the dominant negative CREB transcription factor. Mice were exposed to 20 mg/kg intratracheal PM or PBS at 20 wks. Continuous ECGs (a) and peripheral chemoreflex sensitivity was monitored by diaphragmatic EMG after hyperoxia (b) at 0 and 36 hrs post PM/PBS. Carotid body (CB) sensory responses to hypoxia © and qRT–PCR were performed (d). CREB–PM mice experience increased ventricular arrhythmias (a) (arrhythmia score 5.5 vs 2.2; p= 0.02). Ventilatory depression after hyperoxia (b) is evident in CREB–PM mice indicating altered CB sensitivity. Studies of ex–vivo CB single fibers © reveal enhanced responses to hypoxia in CREB–PM mice.

	CD1–PBS	CD1–PM	CREB–PBS	CREB–PM
b) Neural Minute Ventilation Response to Hyperoxia (% of baseline); n=4	–27.3±1.4	–34.1±1.4	–48.6±2.8	–59.3±4.7
c) CB sensory response to Hypoxia (Δ impulse/sec)	1.2±0.1	2.6±0.5	2.7±0.3	4.3±0.7

(d) Scnn1b, a key CB regulatory gene, is decreased in CBs of CREB–PM mice while the PM marker, IL–6, is upregulated 3000 fold in CREB–PM mice. These data suggest differential effects of PM in the regulation of gene expression in CREB mice. PM not only causes inflammation in the CBs of CREB mice, but dysregulates their function, suggesting a mechanism for arrhythmia development through an autonomic dysfunction pathway.

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